

IN THE UNITED STATES  
PATENT AND TRADEMARK OFFICE

In re Application of :

HIDENORI OHKI et al.

Serial No. : 09/248,267

Art Unit : 1654

Filed : February 11, 1999

Examiner : MARSHALL , S

For : CYCLIC HEXAPEPTIDES HAVING ANTIBIOTIC ACTIVITY

DECLARATION

I, FUMIAKI IKEDA, a citizen of Japan residing at No. 5-1-11, Kisaichi, Katano-shi, OSAKA, JAPAN, declare and say that :

I graduated from Osaka University, Faculty of Pharmacy, in March 1979;

I received the degree of Doctor of Pharmacy from Toho University, in 1987;

Since April 1979 , I have been, as a microbiologist, in the continuous employ of Fujisawa Pharmaceutical Co., Ltd., OSAKA, JAPAN and am now a Senior Research Manager of Medical Biology Research Laboratories;

I received from Mr. Hidenori Ohki the Test compounds 1 to 29, A and B, and I have conducted the anti-microbial tests.

## **Test** (Anti-microbial activity) :

### **Test Method**

In vitro antimicrobial activity of the test compounds was determined by the two-fold agar-plate dilution method.

One loopful of an overnight culture of each test microorganism in Sabourad broth containing 2 % Glucose ( $10^5$  viable cells per ml) was streaked on Sabourad dextrose agar (SDA: dextrose 2%) containing graded concentrations of the test compounds, and the minimal inhibitory concentration (MIC) was expressed in term of  $\mu\text{g/ml}$  after incubation at  $30^\circ\text{C}$  for 24 hours.

**Test Organism** : *C.albicans* FP633

### **Test Result**

No.	MIC ( $\mu\text{g/ml}$ )
A	0.78
B	0.78
1	0.1
2	0.2
3	0.2
4	0.2
5	0.1
6	0.1
7	0.1
8	0.1
9	0.1
10	0.1
11	0.1
12	0.05
13	0.05
14	0.1
15	0.2
16	0.39
17	0.1
18	0.39

No.	MIC (µg/ml)
19	0.39
20	0.2
21	0.2
22	0.2
23	0.05
24	0.1
25	0.1
26	0.2
27	0.2
28	0.39
29	0.39

It is declared by the undersigned that all statements made herein of undersigned's own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements, and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. 1001, and that such willful false statements may jeopardize the validity of this application or any patent issuing thereon.

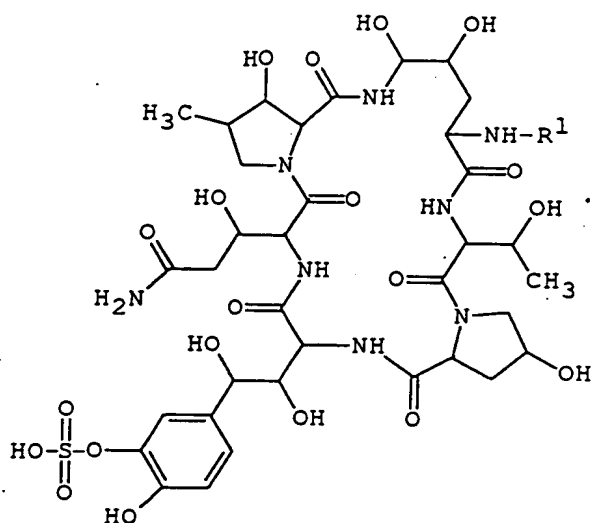
Fumiaki Ikeda  
Fumiaki Ikeda

This 1st day of April, 1999  
OSAKA, JAPAN

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## CLAIMS

1. A polypeptide compound of the following general formula :



wherein  $R^1$  is lower alkanoyl substituted with

*Ex 44* { unsaturated 6-membered heteromonocyclic group containing at least one nitrogen atom which may have one or more suitable substituent(s);

~~lower alkanoyl substituted with 1,2,3,4-tetrahydroisoquinoline which may have one or more suitable substituent(s);~~

*Ex 45* { lower alkanoyl substituted with unsaturated condensed heterocyclic group containing at least one oxygen atom which may have one or more suitable substituent(s);

*Ex 12* { lower alkanoyl substituted with unsaturated condensed heterocyclic group containing 1 to 3 sulfur atom(s)

which may have one or more suitable  
substituent(s);

~~lower alkanoyl substituted with  
unsaturated condensed heterocyclic  
group containing 2 or more nitrogen  
atom(s) which may have one or more  
suitable substituent(s);~~

EX 26

lower alkanoyl substituted with  
saturated 3 to 8 membered  
heteromonocyclic group containing at  
least one nitrogen atom which may have  
one or more suitable substituent(s);

EX 84

ar(lower)alkenoyl substituted with  
aryl which may have one or more  
suitable substituent(s);

EX 21

naphthyl(lower)alkenoyl which may  
have one or more higher alkoxy;

EX 31

lower alkynoyl which may have one or  
more suitable substituent(s);

EX 20

(C<sub>2</sub>-C<sub>6</sub>)alkanoyl substituted with  
naphthyl having higher alkoxy;

EX 16

ar(C<sub>2</sub>-C<sub>6</sub>)alkanoyl substituted with  
aryl having one or more suitable  
substituent(s), in which ar(C<sub>2</sub>-C<sub>6</sub>)-  
alkanoyl may have one or more suitable  
substituent(s);

EX 40

aroyl substituted with heterocyclic  
group which may have one or more  
suitable substituent(s), in which aroyl  
may have one or more suitable  
substituent(s);

~~aroyl substituted with aryl having  
heterocyclic(higher)alkoxy, in which  
heterocyclic group may have one or more  
suitable substituent(s);~~

EX24 ( aroyl substituted with aryl having  
lower alkoxy(higher)alkoxy;

~~aroyl substituted with aryl having  
lower alkenyl(lower)alkoxy;  
aroyl substituted with 2 lower  
alkoxy;~~

EX22 ( aroyl substituted with aryl having  
lower alkyl;

EX35 ( aroyl substituted with aryl having  
higher alkyl;

~~aryloxy(lower)alkanoyl which may have  
one or more suitable substituent(s);~~

EX8 ( ar(lower)alkoxy(lower)alkanoyl which  
may have one or more suitable  
substituent(s);

~~aryl amino(lower)alkanoyl which may  
have one or more suitable  
substituent(s);~~

EX54 ( lower alkanoyl substituted with  
pyrazolyl which has lower alkyl and  
aryl having higher alkoxy;

EX118 ( lower alkoxy(higher)alkanoyl, in  
which higher alkanoyl may have one or  
more suitable substituent(s);

~~aroyl substituted with aryl having  
heterocyclicoxy, in which  
heterocyclicoxy may have one or more  
suitable substituent(s);~~

EX74 ( aroyl substituted with  
cyclo(lower)alkyl having lower alkyl;

EX113 indolylcarbonyl having higher alkyl;

EX82 naphthoyl having lower alkyl;

EX81 naphthoyl having higher alkyl;

~~naphthoyl having lower  
alkoxy(higher)alkoxy;~~

EX103 ( aroyl substituted with aryl having  
lower alkoxy(lower)alkoxy(higher)-  
alkoxy;

EX114 ( aroyl substituted with aryl having  
lower alkoxy(lower)alkoxy;

~~aroyl substituted with aryl which has  
aryl having lower alkoxy;~~

EX89 ( aroyl substituted with aryl which has  
aryl having lower alkoxy(lower)alkoxy;

EX112 ( aroyl substituted with aryl having  
heterocyclicoxy(higher)alkoxy;

EX51 ( aroyl substituted with aryl having  
aryloxy(lower)alkoxy;

~~aroyl substituted with aryl having  
heterocycliccarbonyl(higher)alkoxy;~~

EX109 ( lower alkanoyl substituted with  
oxazolyl which has aryl having higher  
alkoxy;

~~lower alkanoyl substituted with furyl  
which has aryl substituted with aryl  
having lower alkoxy;  
lower alkanoyl substituted with  
triazolyl which has oxo and aryl having  
higher alkyl;~~

EX62 higher alkanoyl having hydroxy;

EX60 ( higher alkanoyl having ar(lower)alkyl  
and hydroxy; or

EX63 3-methyl-tridecenoyl; or

~~(C<sub>2</sub>-C<sub>6</sub>)alkanoyl substituted with aryl  
having higher alkoxy, in which (C<sub>2</sub>-C<sub>6</sub>)-  
alkanoyl may have amino or protected  
amino, and~~

a pharmaceutically acceptable salt thereof.

2. A compound of claim 1, wherein